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TITLE: Rehabilitation of Visual and Perceptual Dysfunction after Severe Traumatic Brain Injury

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
The overall aim is to conduct preliminary evaluations of new rehabilitation strategies and new functional assessment methods for homonymous hemianopia (HH) and spatial neglect (SN), disabling visual and cognitive perception conditions that commonly occur as a result of severe traumatic brain injury (TBI) and stroke. Both HH and SN prevent detection of objects on the affected side, resulting in unsafe walking and driving. Using realistic tasks in virtual environments representative of everyday mobility challenges we are evaluating a novel optical device – expansion prism (EP) glasses - combined with a new computerized perceptual-motor training regimen in helping people with HH and SN detect and avoid obstacles on the affected side. In the first year we developed the training software and prepared the functional assessments. In the second year we have made excellent progress in recruiting and running participants in the main pilot study, with a total of 25 participants screened and 14 enrolled. There are about 15 visits for each participant, including about 6 visits for intensive computerized perceptual-motor training. Preliminary results are encouraging. After training there were significant improvements in the ability to accurately touch targets presented in areas of prism-expanded vision in the blind hemifield. Before training, the error in touching was 17º, which reduced significantly (p = 0.001) to only 1.0º after training (equivalent to seeing side accuracy). Blindside detection performance improved significantly when using the prism glasses both in a collision judgment task in a virtual walking simulator and a pedestrian detection task in a driving simulator. Recruitment and data collection are ongoing.

15. SUBJECT TERMS
Hemianopia; spatial neglect; prismatic corrections; adaptation; perceptual-motor training; rehabilitation; mobility; functional outcome measures

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INTRODUCTION

Rehabilitation of Visual and Perceptual Dysfunction after Severe Traumatic Brain Injury
The aim of our project is to conduct preliminary evaluations of new rehabilitation strategies and new functional assessment methods for homonymous hemianopia (HH) and spatial neglect (SN), disabling visual and cognitive perception conditions that commonly occur as a result of severe traumatic brain injury (TBI) and stroke. Both HH and SN prevent detection of objects on the affected side, resulting in unsafe walking and driving. In our pilot study we are evaluating a novel optical device combined with a new computerized perceptual-motor training regimen in helping people with HH and SN detect and avoid obstacles on the affected side. The optical device, expansion prism (EP) glasses, uses high power prism segments embedded in a regular spectacle lens to project areas from the affected (blind/neglected) side onto the unaffected (seeing) side while leaving central vision uninterrupted. The purpose of the perceptual-motor training is to help people learn how to interpret the information from the peripheral prisms so that they can correctly identify the location of objects detected via the prisms and respond appropriately (e.g., avoid a collision when walking or turn to face a person approaching on the blind/neglected side). The effects of the EP glasses and training is being evaluated using realistic tasks representative of everyday mobility challenges including detection of pedestrian hazards in a driving simulator and obstacle collision judgments in a virtual mall. In addition, this project addresses another important basic research question; namely, the effect of the interventions on eye movement behaviors. Eye movements are being measured without and with EP glasses and after training in the driving simulator, the collision judgment task and a natural walking task. The eye movement data will provide a basic understanding of how participants are using the device and will help guide future developments of prismatic devices for HH and SN.

BODY

I. Task 1 - Preparation of study protocols.
This task was completed in year 1.

II. Task 2 - Complete development of the perceptual-motor training program
This task was mostly conducted in year 1. However, throughout year 2 we have continued to add additional enhancements to the program, fixes to previously hidden bugs, and modifications to allow greater flexibility and ease of use, and improve the more complex aspects of the training. This task is now finished.

Accomplishments
- The program now includes five levels of training and has been used extensively for training sessions in the main pilot study (Task 5).
- We have implemented animated user feedback screens, a template task for each level of training that simplifies setting up new tasks, the use of video as a fixation target and multiple default prism zones per subject with integrity checking.
- In addition, we have extended the training to more real-world situations by incorporating detection of natural hazards in natural driving videos.

III. Task 3 – Functional assessments in the driving simulator and virtual mall
In year 1 we completed the modification and testing of existing scenarios in the driving simulator (detection of potential pedestrian hazards) and the existing collision judgment task in the virtual-mall walking simulator. In year 2, both the driving simulator and virtual mall tasks have been successfully deployed in the main pilot study. Our efforts under this task in year 2 have mainly focused on the eye and head tracking aspects, as well as the development of data analysis programs.

Accomplishments – Driving simulator
- We have modified existing data analysis programs for analyzing detection performance in the driving simulator, including detection rates and reaction times, and are in the process of adding the capability to

determine the proportion of pedestrian appearances for which there would have been a collision in the real world (missed detections and very late responses).
- We are also in the process of modifying existing programs to evaluate lane position and steering.
- We have streamlined the driving simulator data analysis process and have added capability to the data analysis program to produce customized, publication quality plots of gaze.
- We have devoted much effort to implementing calibration tests and verification procedures for the SmartEye eye and head tracking system that we are using to record eye and head movements when driving with and without prism glasses so that we can determine how participants are using the EP glasses and the effects of perceptual-motor training on eye movement behaviors.
- We have also been working on developing an algorithm to quantify eye and head movement behaviors in the driving simulator. The algorithm has been applied to the data from one participant and now needs to be run on the complete data set.

Accomplishments – Virtual mall walking simulator
- We have added new features to the existing collision judgment program including "catch trials" (trials without a target), a calibration feature, and an option for manually tagging data when a fixation loss occurs.
- We have been developing data consolidation programs and also data analysis programs, in particular for collision judgment responses that cannot be fit with a cumulative Gaussian.
- As participants perform some of the collision judgments with fixed gaze, we have developed a program for monitoring fixation. The first implementation was with an old remote IR eye tracker (ISCAN), which we subsequently replaced with a SmartEye head and eye tracker released from another experimental set up.

IV. Task 4 - Outdoor walking task
We have made much progress on this task in the last 12 months. At the beginning of year 2 we purchased a PositiveScience eye tracker and associated software and by the end of the first quarter had implemented it in the main pilot study. Eye and head movements are now being routinely recorded while patients walk a short outdoor route.

Accomplishments
- We completed setting up the Positive Science eye tracker and two separate motion sensors for recording of head position relative to the body when walking, developed calibration procedures, finalized two outdoor walking routes, received training from an orientation and mobility specialist, and then started to collect eye and head position data from all participants in the pilot study.
- We received a new computer from Schepens (at no cost) with which we developed a system for backing-up, processing, and analyzing the approximately 150 GB per month of eye and head movement data collected.
- We have been processing eye and head movement data, and are currently developing a method of integrating them (not a trivial task) so that we can analyze scanning behaviors based on gaze direction.

V. Task 5- Pilot study EP glasses and training
Our main focus in year 2 has been on recruiting and running participants in the pilot study. We have made good progress despite one research assistant leaving and another starting in the second quarter of the year. The whole study involves at least 15 visits per participant. This year we have run 219 patient visits, a total contact time of about 550 hours. Our original statement of work was for 2 years, but we have been granted a no cost extension for an additional year so that we can complete data collection for the main pilot study.

Enrollment
The aim is to have 12 patients with HH without SN and 12 patients with HH with SN complete the pilot study. Allowing for attrition, a total of 15 patients with HH without SN and 15 patients with HH with SN were approved for participation.

In the last 12 months we have prioritized recruitment of patients with HH without SN in order to reach our goal of 12 patients to complete the whole study. We have also established routes of referral for patients with HH with SN (Dr Houston will refer patients from his clinic at Spaulding Rehabilitation Hospital). We will focus on recruitment of patients with SN when the cohort of patients without SN has completed all training visits. (Due to the large number of visits, we can only reasonably accommodate two patients in training at the same time).

HH without SN
- In total, since the start of the study, 22 patients with HH without SN have been screened for the main pilot study of which 13 met the criteria and have been enrolled in the study; 5 have completed the protocol, 7 are part way through the protocol, 1 withdrew and 0 are currently lost to follow up.
- Of these, 12 were enrolled within the last 12 months.

HH with SN
- In total, since the start of the study, 3 patients with HH with SN have been screened for the main pilot study of which 1 met the criteria and was enrolled and completed the study.

Enrollment for each protocol since the start of the study:

Table 1: Screened, met the study criteria and enrolled in the main pilot study, as of 02/28/2013

Schepens IRB protocol number	HRPO Log Number	Hemianopia Without neglect	Hemianopia With neglect	Normal vision
2011-07 (Prism Training)	A-16638.1	13	1	0
2011-09 (Eye movements outdoors)	A-16638.2	7	1	0
2011-010 (Virtual walking sim)	A-16638.3	9	1	0
2011-011 (Driving sim)	A-16638.4	11	1	0

Table 2: Screened, but did <u>not</u> meet the study criteria, as of 02/28/2013
(These subjects do not count toward the total number approved)
The main reason for not meeting the study criteria was incomplete hemianopia. Some of the patients who did not meet the criteria, but still had substantial visual field loss, were invited to participate in pre-pilot work when we were refining our methodology in preparation and refinement of the tools for the main pilot study.

Schepens IRB protocol number	HRPO Log Number	Participated in pre-pilots		Did not participate	
		Without neglect	With neglect	Without neglect	With neglect
2011-07 (Prism Training)	A-16638.1	5	1	3	1
2011-09 (Eye movements outdoors)	A-16638.2	0	0	0	0

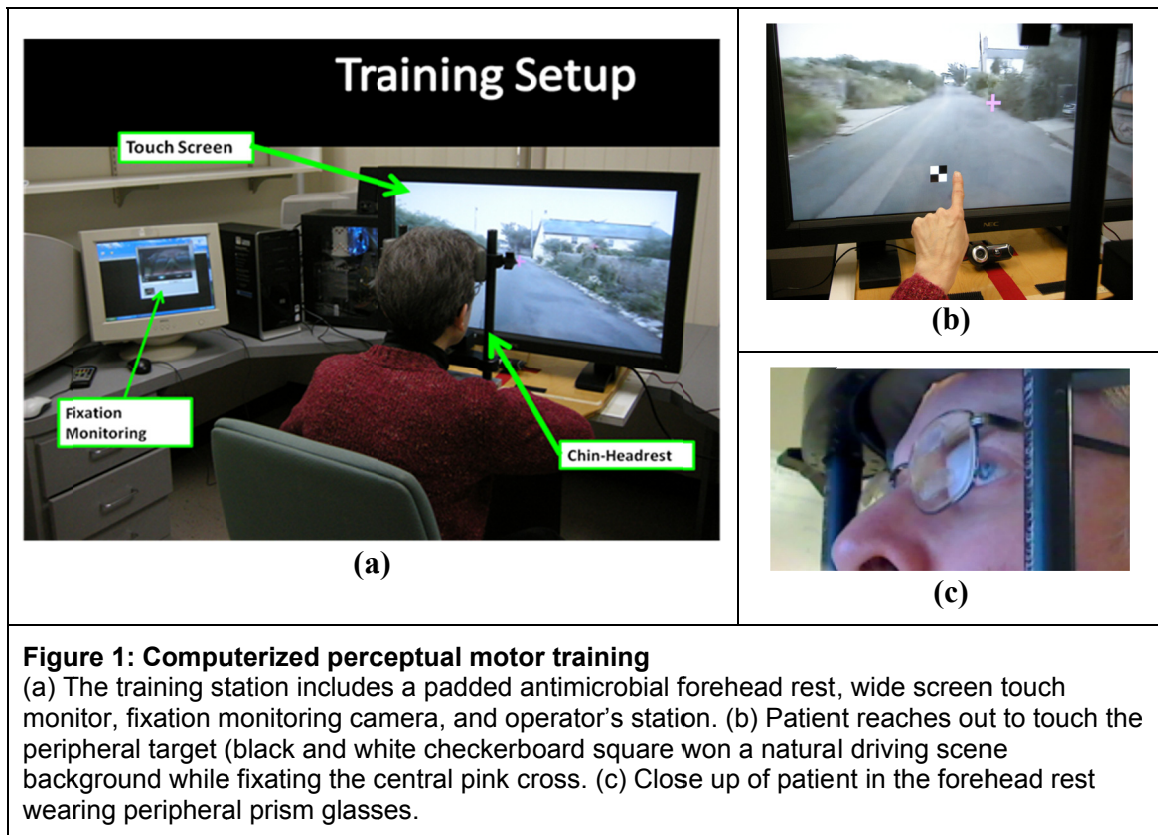|						
2011-010 (Virtual walking sim)	A-16638.3	4	2	0	0
2011-011 (Driving sim)	A-16638.4	3	2	0	0

Preliminary data
Below we report preliminary data for each of the main aspects of the pilot study.

A. Perceptual Motor Training
This training involves, while wearing the prism glasses, reaching out and touching (on a touch screen) peripheral objects displayed on the blind/neglected side and on the seeing side of the visual field while maintaining fixation on a central target (Figure 1).
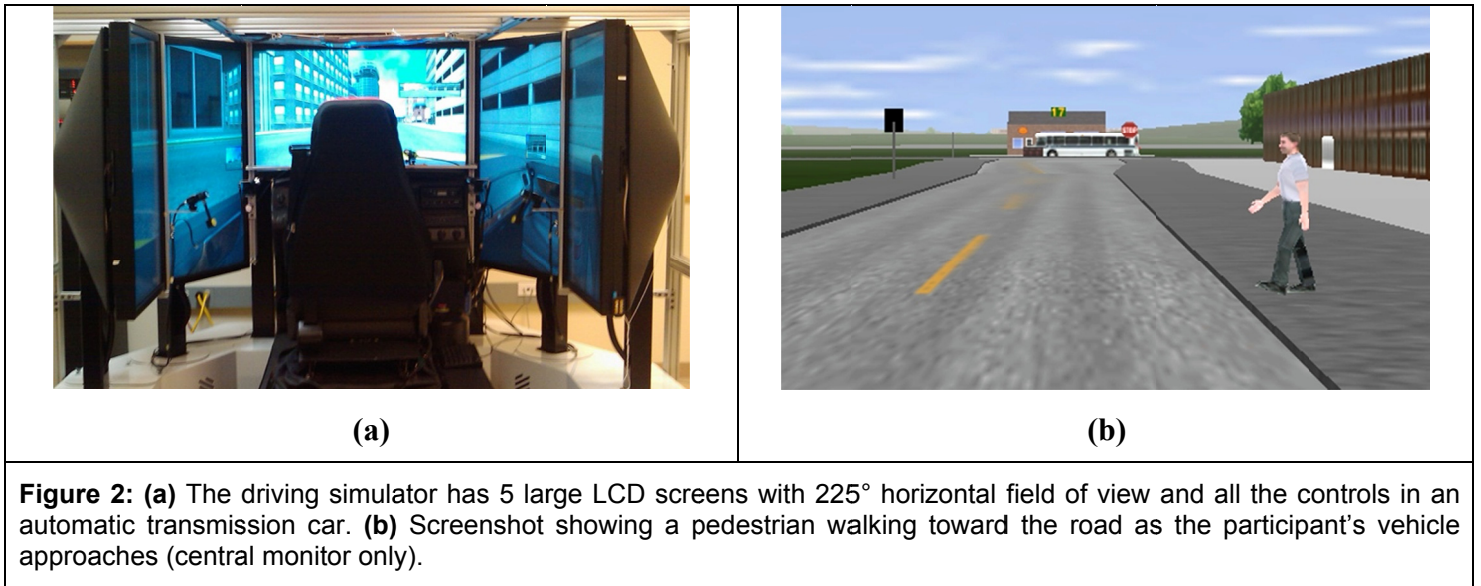
In the last 12 months, 7 participants with hemianopia without neglect have completed the full training schedule, with significant improvements in the ability to accurately touch targets presented in areas of prism-expanded vision in the blind hemifield. Before training, the error in touching was 17º, which reduced significantly (p = 0.001) to only 1.0º after training (equivalent to seeing side accuracy). Furthermore, the difference between seeing and prism side reaction times reduced significantly (p=0.04) from 876ms to 110ms. These results are encouraging.

Figure 1: Computerized perceptual motor training
(a) The training station includes a padded antimicrobial forehead rest, wide screen touch monitor, fixation monitoring camera, and operator's station. (b) Patient reaches out to touch the peripheral target (black and white checkerboard square won a natural driving scene background while fixating the central pink cross. (c) Close up of patient in the forehead rest wearing peripheral prism glasses.

B. Driving simulator
Each driving simulator assessment comprises five test drives (each about 10 minutes) on pre-determined routes guided by computer-generated, spoken navigation cues (similar to GPS instructions) (Figure 2a). While driving, the participant's primary task is to press the horn button whenever he/she detects a pedestrian figure that

appears periodically at small and large eccentricities on the right and left of the roadway (Figure 2b). The pedestrian figures move with biological motion toward the road on a collision course, but do not enter the travel lane. The driving is highly engaging as there is other traffic on the roads and the participants have to obey all the normal rules of the road. Main outcome measures are detection rates and reaction times.

(a) **(b)**

Figure 2: (a) The driving simulator has 5 large LCD screens with 225° horizontal field of view and all the controls in an automatic transmission car. **(b)** Screenshot showing a pedestrian walking toward the road as the participant's vehicle approaches (central monitor only).

Preliminary results for 9 participants with hemianopia without neglect suggest a significant improvement in detection of blind side pedestrian hazards with the prism glasses following training. Median blindside detection rates for approaching pedestrian hazards improved from 63% without prism glasses to 88% with prism glasses ($p = 0.011$; Figure 3).
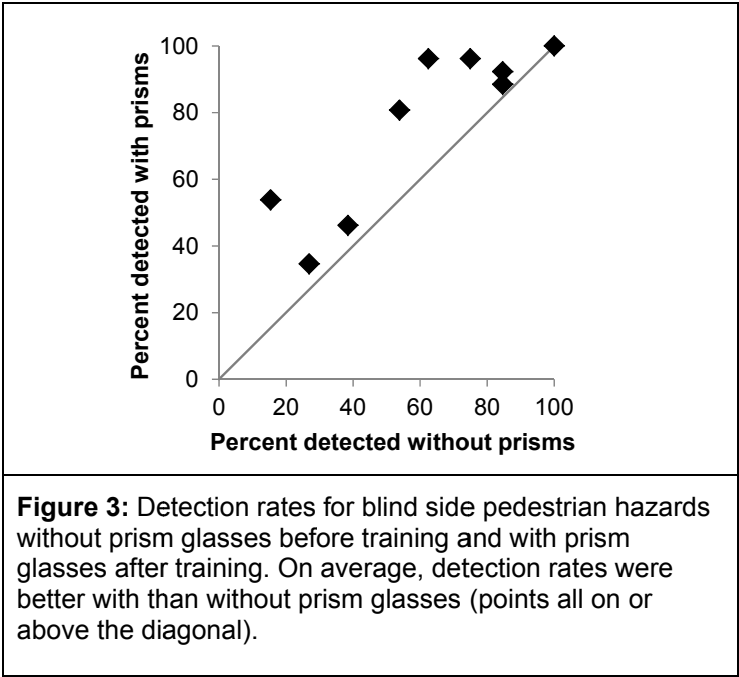

Figure 3: Detection rates for blind side pedestrian hazards without prism glasses before training and with prism glasses after training. On average, detection rates were better with than without prism glasses (points all on or above the diagonal).

C. Collision judgments in virtual mall walking simulator

The virtual mall is a virtual reality model of a real shopping mall (Figure 4). Participants are 1m in front of a large rear-projection screen on which the shopping mall is displayed. Their task is to report whether they would collide with stationary obstacles (life-sized human figures; Figure 4) that periodically appear at different offsets (up to 120cm to each side) from the simulated participant's walking direction. Outcome measures are detection rates for obstacles, the perceived safe passing distance on the blind and seeing sides, and judgment uncertainty.
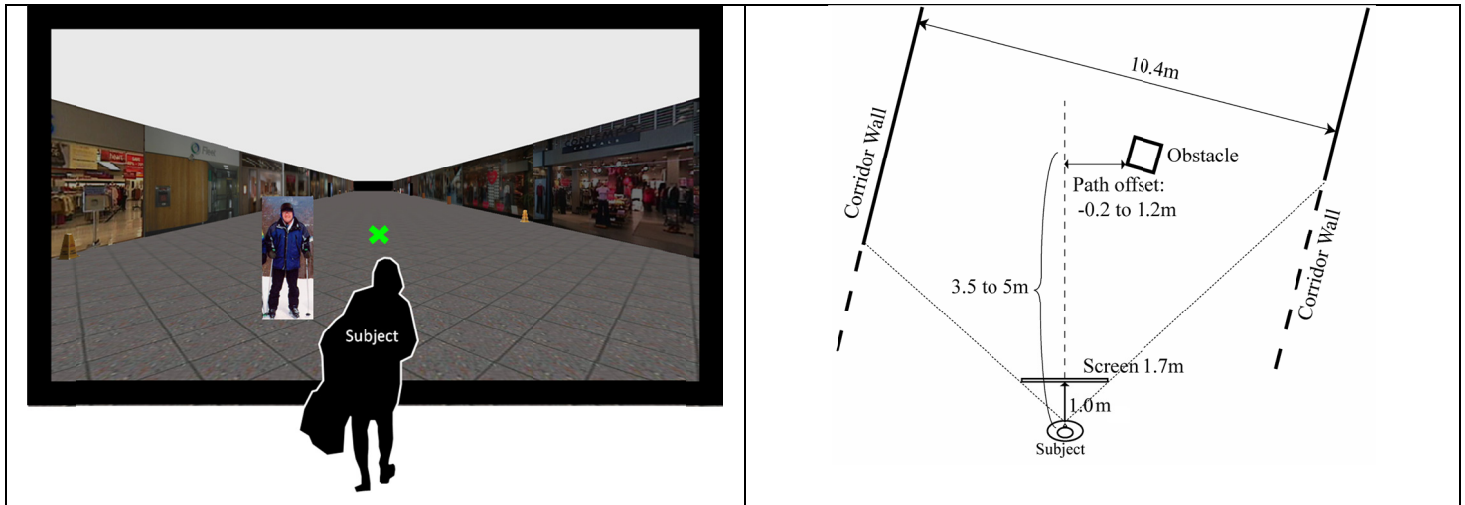

Figure 4. Illustration of the virtual reality mall set-up and collision judgment task.
Participants are instructed to fixate a cross at the center of the screen (green x) and imagine that they are walking in a real shopping mall. A figure appears, moves in a linear path, and disappears after 1 second. The participant clicks a button when they detect the figure and then responds verbally "collision", "no collision", or "nothing" for each trial. The figure may appear at any eccentricity offset to the right or left of center, or not at all (10% of trials). This is repeated for a total of 88 trials.

For conditions in which participants fixated a central cross on the screen, blindside detection rates were significantly better with than without the prism glasses (improved by 59% with prism glasses, p = 0.01). In addition, under natural scanning conditions, detection rates also increased with the prism glasses (by 18%) to a median of 100%. When wearing the prism glasses, detection rates on the blind side were as good as those on the seeing side. Collision judgments for pedestrians in the blind hemifield made from the prism-expanded vision differed from collision judgments on the seeing side. As the data for judgments in the blind hemifield cannot be adequately fit by a traditional psychometric function (unlike seeing side judgments), we are currently developing an algorithm to quantify blind hemifield collision judgments when using the prism glasses.

D. Eye and head movements when walking outdoors

Using the integrated eye and head tracking system (Figure 5), we have collected and processed data for 7 subjects with hemianopia without neglect. Each participant walked short outdoor routes along busy downtown Boston streets. Figure 6a shows an example of the output for the gaze tracking of a right hemianope during a 17 s period from a walk without prism glasses. To derive the gaze position (red line in Figure 6), the eye movement data were synchronized and added to the head position information (blue line in Figure 6).

We have conducted a preliminary analysis of the gaze data from two visits for each subject, including with- and without- prism walks at each visit. Gaze movements were analyzed within the blind and seeing hemifields as the sum of the gaze movement amplitudes divided by the total number of samples. Patients had a trend to bias their gaze position towards the blind side when wearing the prisms but not when walking without them (significant side*prism interaction, p=0.009). This suggests that, due to the prisms, the patient's attention was attracted to their blind side (as indicated by the gaze direction). As yet we have insufficient data to evaluate the effects of training on gaze behaviors.

Figure 5: (a) The mobile gaze tracking system including two motion sensors to measure head position relative to body position, the Positive Science eye tracker and two small notebook computers for data recording. (b) Close up of the eye tracker eye and scene cameras mounted on a custom frame suitable for the mounting of prism lenses.
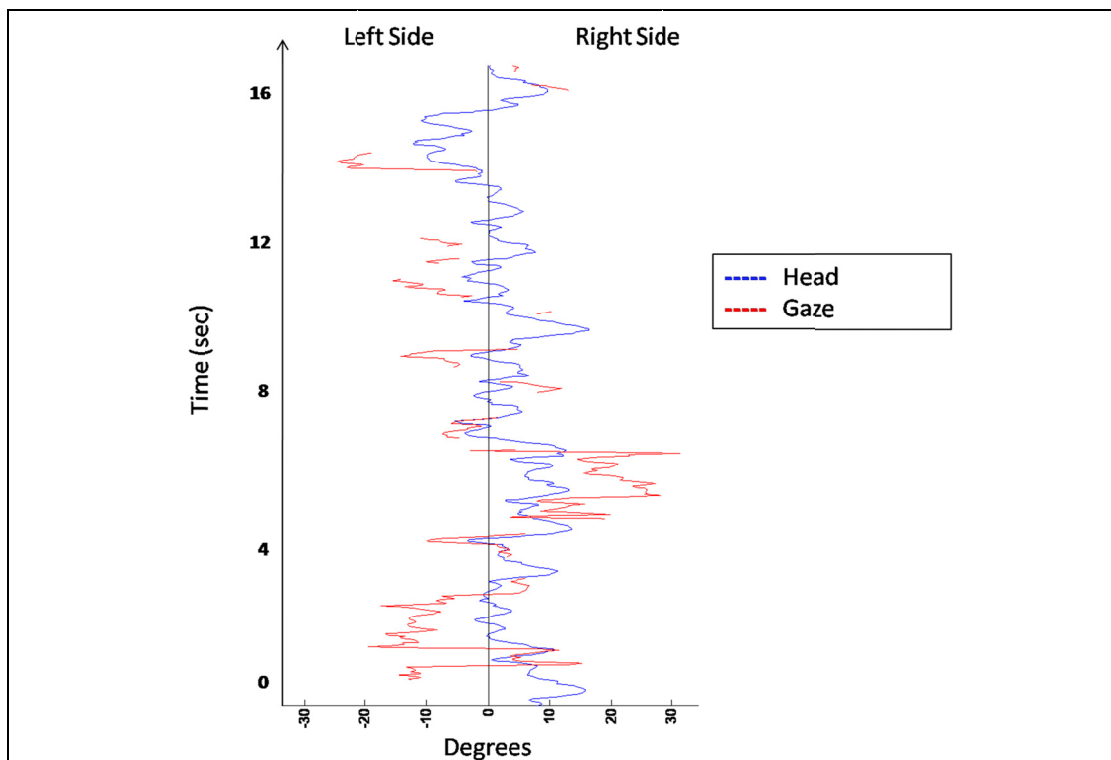

Figure 6. Gaze data of a patient with right hemianopia when walking without prism glasses. Eye position data are synchronized and combined with the head position data (blue line) to give gaze direction (red line)

KEY RESEARCH ACCOMPLISHMENTS

In months 12 to 24, we have:
- Renewed all necessary IRB approvals;
- Made excellent progress in recruitment and running participants with HH without SN and are nicely on track to have 12 participants in this group complete the study;
- Made much progress in the head and eye tracking aspects of the project, in particular for the outdoor walking task.

REPORTABLE OUTCOMES

- Preliminary data for the virtual-mall walking-simulator collision detection task was presented at the American Academy of Optometry 2012 meeting in October.
- An abstract reporting preliminary data from the prism training and pre- and post-training results from the virtual-mall walking-simulator collision detection task has been accepted for a poster presentation at ARVO 2013 (Association for Research in Vision and Ophthalmology).
- An abstract reporting preliminary data from the outdoor walking task has been accepted for a poster presentation at ARVO 2013
- Dr Houston gave an invited talk at the New England College of Optometry about the methodology and early results from the study
- Dr Luo's postdoctoral fellow gave a talk at Schepens about the development of the outdoor eye and head tracking methodology and preliminary results.
- Three papers are in preparation: a paper addressing the development of the prism-training methodology, a paper reporting data from the collision judgment task in the virtual-mall walking-simulator, and a paper addressing the methodology for integrating eye and head movement data from the outdoor walking task.

CONCLUSIONS

In this second year we have made excellent progress in recruiting and running participants with hemianopia without neglect. We are clearly on track to reach our goal of 12 participants with hemianopia without neglect to complete the whole study, with 5 already completed and 7 currently part way through the protocol. We have also established routes of referral for patients with hemianopia with neglect and will start to increase recruitment of these patients when the cohort without neglect has completed all training visits.

REFERENCES

None

APPENDICES

None